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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/637,216	08/11/00	HULTGREN S	WSHU2005.1

000321 HM12/0913
SENNIGER POWERS LEAVITT AND ROEDEL
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS MO 63102

EXAMINER	
SHEIKHERZ, M	
ART UNIT	**PAPER NUMBER**
1631	14

DATE MAILED: 09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/637,216	HULTGREN ET AL.	
	Examiner	Art Unit	
	Monika B. Sheinberg	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 20, 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-135* is/are pending in the application.

4a) Of the above claim(s) *3, 18, and 22-135* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-17, and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-135* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 sheets* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Attachment to PTO-948

DETAILED ACTION

Response to Restriction/Election

Applicant's election with traverse of Group I (claims 1, 2, 4-17, and 19-21) and of species elections: a peptide compound, Escherichia coli, formula I, and SEQ ID No: 12; of in Paper No. 12, filed on June 20, 2001, is acknowledged.

The traversal of Group I is on the ground(s) that the search and examination of the entire fourteen groups or at least some are under the same classifications. This is not found persuasive because these inventions are distinct for the reasons stated within the restriction requirement. Even though groups fell within similar classifications, such as Groups I, II, II and XI, are each compositions that can stand alone, and do not require the presence of one of the others. In addition, the broad and general search of Group I, an isolated compound, would not produce results with such varied limitations that Groups II, III, and XI contain. Thus a search on one of these compositions will not necessarily bring about art on each and every other composition listed. The fourteen inventions are not coextensive in scope and would pose an undue burden upon the examiner to perform fourteen different searches and provided art to each and every one. As by U.S. Patent Law, "one invention, one patent".

The species traversal is on the grounds that the two formulas provided all generally are directed to pilus subunit groove binding, and that all the compounds exhibit antibacterial activity against all Gram-negative bacteria. The arguments against the formula speciation are not found persuasive because they each contain their own distinct sequences. Thus this results in non-overlapping sequence search characteristics. In addition, it is well known in peptide/protein

subject matter that as distinct sequences, they will result in distinct folding states while in their functional form. The arguments against the Gram-negative bacteria speciation are not found persuasive because if the applicant states that the compounds exhibit antibacterial activity against all strains of Gram-negative bacterium, it is confusing why the applicant is claiming separate organisms if they all display the same behavior. In addition, it is well known that generally antibiotic publications are focused on a particular bacterial species and only infrequently are all Gram-negative bacterium analyzed together. Bacteria are given different names due to their distinct characteristics and corresponding different biochemical characteristics which most commonly contain different and distinct antibiotic reactions.

Because these fourteen inventions are distinct for the reasons given in Paper No. 10, filed on March 7, 2001, and the search required for Group I (an isolated compound), for example is not required for Group V (method of preventing or inhibiting formation of a chaperone-subunit structure in a subject), restriction for examination purposes as indicated is proper. In addition, because the plurality of disclosed patentably distinct species are different and distinct as discussed above, the species requirement as indicated is proper.

All the restriction and species election requirements are still deemed proper and are therefore made FINAL.

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title includes co-crystals of pilus subunits an methods of use thereof, whereas the elected claims are directed only to the antibacterial compounds.

Drawings Notice

Applicant is hereby notified that the required timing for the correction of drawings has changed. See the last 6 lines on the sheet which is attached entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". It is noted that a PTO Form 948 was mailed with Paper No. 10 on March 7, 2001. Due to the above notification Applicant is required to submit drawing corrections within the time period set for responding to this Office action. *Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.*

Claim Rejections - 35 USC § 112

The following is a quotation of the ***first*** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6)

the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant application lacks any amount or direction as to the practice of utilizing the G_1 beta strand of claim 4, since the G_1 beta strand is not defined in the disclosure. Nowhere in the claims or the specification is there a clear and direct explanation as to what exactly the G_1 beta strand is. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of working examples in the specification, and the unpredictability of the selecting a beta strand in the context of a complex or simple molecule, the specification, as filed is not enabling for the G_1 beta strand. As such, claims (4-7) drawn to the practice of G_1 beta strand are not enabled.

The following is a quotation of the ***second*** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-7, 12-15, 20, and 21, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of G_1 beta strand of claim 4 are not defined within the instant disclosure, and thus renders the claim vague and indefinite, as with all claims that are drawn to the practice of the G_1 beta strand (claims 4-7).

Claim 5, 12-15, 20, and 21, lack a clear and concise definition of the metes and bounds of "analogue" or "analog". The lack of clarity allows an interpretation of the claim language "analogue" to mean a peptide. Reasonably the peptide interpreted can be any peptide. The extent of what defines the analogue similarity between peptides is unclear, as well as between mannose molecules. Claims 13-15 are rendered vague and indefinite due their dependency from claim 12.

Claim Rejections - 35 USC § 102/ 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-17, and 19-21, are rejected under 35 U.S.C. 102(b) as anticipated by Marklund et al. (*Mol. Microbiol.,* 1992)

Marklund et al. has the following peptide, SEQ ID No: 12 entered into an NIH database (Protein Identification Resource) as accession #: S16400 (see attached sequence print-out). The reference clearly displays on page 2229 of their figure 1, the sequence attained from the species election, E. coli; just as the claimed isolated compound. Under U.S. Patent Law: "a claim in a patent application directed to an old compound in the art does not become patentable merely by measuring a new characteristic thereof", such as the claimed pilus assembly inhibition. As such any claims that are drawn to the practice of SEQ ID No: 12, the isolated compound, are rejected.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to

believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claims 1, 2, 4-17, and 19-21, are rejected under 35 U.S.C. 102(b) as anticipated by Marklund et al. or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kuehn et al. (*Science*, 1993).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

The mimic of the isolated compound that comprises the SEQ ID No: 1 (papD) or an analogue thereof can be any of the listed compounds in the reference, Kuehn et al., due to the lack of clarity of the metes and bounds of "analogue". Thus, the mimic of claims 4-7 is anticipated by the reference.

Kuehn et al. motivates on page 1235-36, the modifications as stated in claim 6 and 9, determined the abilities of the peptides, including SEQ ID No: 12, papK, to inhibit the papD chaperone, SEQ ID No: 1. As summarized in the reference on page 1240 (last paragraph):

> ... the mode of chaperone binding described in this article actually presents a "snapshot" of a process fundamental to Gram-negative pathogens. The molecular details of the charperone-adhesin interaction and optimization... may lead to the design of high affinity synthetic inhibitors which would prevent pilus assembly...

The entire reference clearly motivates instant invention in context of chaperones, pilus assembly inhibition, mimics ("any short peptides sufficient for binding" –bridging phrase of page 1235-1236), complexes compromising of pili or Pap D peptides, and the Gram-negative bacterium (E.coli).

No claim is allowed.

Closure

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

ARDIN H. MARSCHEL
PRIMARY EXAMINER

August 31, 2001

Monika B. Sheinberg
Patent Examiner
Art Unit 1631

MBS

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.